(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 17 February 2005 (17.02.2005)

PCT

(10) International Publication Number WO 2005/014775 A3

(51) International Patent Classification⁷:
A61K 48/00

A01N 63/00,

(21) International Application Number:

PCT/US2003/020746

(22) International Filing Date:

30 June 2003 (30.06.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/392,725

28 June 2002 (28.06.2002) US

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(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

(88) Date of publication of the international search report: 2 February 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: RAAV COMPOSITIONS AND METHODS FOR DELIVERY OF HUMAN FACTOR VII POLYPEPTIDES AND TREATMENT OF HEMOPHILIA Λ

(57) Abstract: Disclosed are improved recombinant adeno-associated viral (rAAV) vector compositions useful in the delivery of antihemophilic factor polypeptides to selected mammalian host cells. The disclosed rAAV vector compositions preferably comprise one or more polynucleotide sequences that express one or more mammalian Factor VII proteins, polypeptides, peptides, a operably linked to one or more promoter and/or enhancer sequences that are capable of expressing the encoded antihemophilic therapeutics in cells suitably transformed with the disclosed rAAV vector constructs, virions, and viral particles comprising the contructs of interest. These compositions, and methods for their use, including the manufacture of medicaments, have desirable therapeutic and/or prophylactic efficacy in the amelioration, treatment, and/or prevention of a variety of diseases, disorders, and dysfunctions in selected mammals, and in particular, humans diagnosed with Factor VII deficiency and/or hemophilia A.



International application No.

PCT/US03/20746

ACLASSIFICATION OF SUBJECT MATTER PECTY): ADIN 53/09, SAIK 48/09 US CL: 42493.2 According to laterastical Patent Classification (PC) or to both national classification symbols) US : 42493.2 Documentation searched (classification system followed by classification symbols) US : 42493.2 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched place of the search of			10.000			
PCCT) : A01N 63/00, A61K 48/00 US CL: 42/493.2 According to International Patent Classification (IPC) or to both national classification symbols) US: +24/93.2 Documentation searched Other than minimum documentation to the extent that such documenta are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet C. DOCUMENTS CONSIDERED TO BE RELEVANT Category* Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Totogory* MARGARITS et al. Long-term expression of activated FVII in vivo fallowing AAV- modiated liver gene transfer: implications for treatment infusion of recombinant activated FVII Blood. November 2001, Vol 98. No. 11 Part 1, page 696s, abstract 2008. X US 6,132,729 A (THORPE et al.) 17 October 2000 (17.10.2000), see whole document, especially pages 34.6. **Special categories of cited documents - specially pages 14.6. **Purther documents are listed in the continuation of Box C. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **Special categories of cited documents - specially pages 34.6. **A document within my draw document and the cited to such document of a categories of the cited the special pages 34.6. **A document depth my draw document of the cited to special pages 34.6. **A document depth my draw document of the	A. CLAS	SIFICATION OF SUBJECT MATTER				
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PCT/US03/20746

The special technical feature of group II is considered to be SEQ ID NO: 8. The special technical feature of group III is considered to be SEQ ID NO: 10. The special technical feature of group IV is considered to be SEQ ID NO: 12. The special technical feature of group V is considered to be SEQ ID NO: 14.
The special technical feature of group VI is considered to be SEQ ID NO: 15. The special technical feature of group VII is considered to be SEQ ID NO: 17.

Accordingly, Group I-VII are not so linked by the same or a corresponding technical feature as to form a single general inventive concept.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: I) each variant has a different mode of action; and II) each variant has a different mode of action.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, STN

search terms: AAV, Factor VII, FVII, hemophilia, adeno associated virus

International application No.

PCT/US03/20746

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)			
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:			
1. Claim Nos.: because they relate to subject matter not required to be searched by this Authority, namely:			
Claim Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to su an extent that no meaningful international search can be carried out, specifically.	ah .		
3. Claim Nos.: 51-64 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)			
This International Searching Authority found multiple inventions in this international application, as follows: Please See Continuation Sheet			
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims. 2. As all searchable claims could be searched without effort justifying an additional fee, this Anthority did not invite payment of any additional fee. 3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:			
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-50 (SEQ ID NO: 1 and 2) Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.			

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-50, drawn to a recombinant adeno-associated viral (AAV) vector comprising a nucleic acid set forth in SEQ ID NO: 1 or a nucleic acid encoding a human Factor VII peptide set forth in SEQ ID NO: 2.

Group II, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid set forth in SEQ ID NO: 7 or a nucleic acid encoding a rat Factor VII peptide set forth in SEQ ID NO: 8.

Group III, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid set forth in SEQ ID NO: 9 or a nucleic acid encoding a danio Factor VII peptide set forth in SEQ ID NO: 10.

Group IV, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid set forth in SEQ ID NO: 11 or a nucleic acid encoding a murine Factor VII peptide set forth in SEQ ID NO: 12.

Group V, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid set forth in SEQ ID NO: 13 or a nucleic acid encoding a chicken Factor VII peptide set forth in SEQ ID NO: 14.

Group VI, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid encoding a rabbit Factor VII peptide set forth in SEQ ID NO: 15.

Group VII, claim(s) 1-9, 11-16, 18-30, and 36-50, drawn to a recombinant adeno-associated viral vector comprising a nucleic acid encoding a bovine Factor VII peptide set forth in SEQ ID NO: 17.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I:

I) SEQ ID NO: 3 and 4; and II) SEQ ID NO: 5 and 6.

The claims are deemed to correspond to the species listed above in the following manner:

I) claims 3-8, 11-16, 27-30; and II) claims 3-8, 11-16, 27-30.

The following claim(s) are generic: claims 1, 2, 9, 18-26, and 36-50.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-VII appears to be that they all relate to an AAV vector comprising a nucleic acid encoding a Factor VII peptide.

However US 5,789,390 (4-8-98) teaches an AAV vector comprising a nucleic acid encoding Factor VII peptide.

Therefore, the technical feature linking the inventions of Groups I-VII does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The special technical feature of group I is considered to be SEQ ID NO: 2.